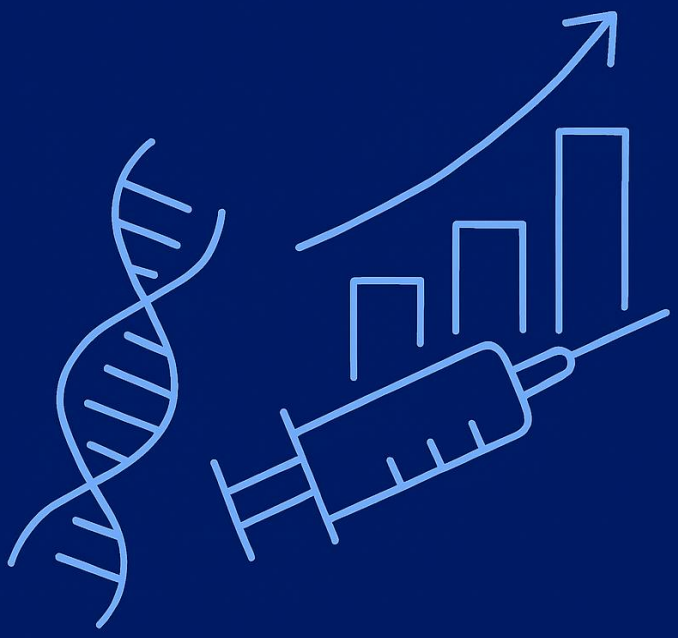
World Health Organization

Meeting Report:

Initial Discussions on Investment Opportunities for mRNA Technology in Low and Middle-Income Countries



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Contents

Abbreviations and Acronyms

AIIB – Asian Infrastructure Investment Bank

CAPEX – capital expenditure

DFI – development finance institution

GMP – Good Manufacturing Practice

IDB – Inter-American Development Bank

IFC – International Finance Corporation

LMICs – low- and middle-income countries

MDBs – multilateral development banks

mRNA – messenger ribonucleic acid

mRNA TT Programme – mRNA Technology Transfer Programme

PAHO – Pan American Health Organization

R&D – research and development

WHO – World Health Organization

Executive Summary

On April 17, 2024, during the World Bank Spring Meetings, WHO, PAHO, and MPP convened a hybrid meeting to discuss financing mRNA-based technologies in LMICs. The meeting aimed to engage multilateral development banks (MDBs) and stakeholders in supporting the expansion of vaccine production and pandemic preparedness. The meeting aimed to explore investment opportunities in mRNA technology in Low and Middle-Income Countries (LMICs). The COVID-19 pandemic highlighted the disparities in vaccine distribution, emphasizing the need for localized production to improve global health equity. The mRNA Technology Transfer Programme (mRNA TT Programme), launched in 2021 by WHO seeks to build local capacity for mRNA vaccine development and manufacturing.

Key Sessions and Discussions

Investment Models of MDBs for Local Manufacturing:

MDBs presented funding instruments for health product development in LMICs, emphasizing the need for an integrated ecosystem for sustainable vaccine manufacturing. Panelists discussed challenges like technology risks, the need for higher risk appetite, and collaborative efforts among MDBs to support local manufacturers. Innovative financing mechanisms, such as blended finance and milestone payments, were proposed to foster commercial viability and sustainability.

CAPEX-OPEX Models and Pandemic Response Capacity:

An analysis of capital and operational expenditures for mRNA vaccine production facilities was presented, highlighting different investment scenarios. The potential contribution of the mRNA TT Programme to pandemic response was discussed, with projections indicating significant vaccine production capacity within a decade.

Building Ecosystems for New mRNA Products:

Panelists addressed the R&D ecosystem for mRNA products, emphasizing the importance of sustainable investment in both pandemic and endemic disease targets. Representatives from Afrigen and IPT shared their experiences in securing investments and building capacity for mRNA technology, highlighting challenges and successful strategies.

Financing LMIC-Based Manufacturers:

Discussions focused on reducing barriers for new manufacturers to secure funding, advocating for a blended approach combining grant funding and MDB/DFI financing. Panelists emphasized the importance of strategic partnerships and diverse funding sources, including angel investors and crowdfunding initiatives.

Key Themes and Recommendations

Collaborative Efforts: Collaboration between MDBs, private financiers, and public sector funders is crucial for sustainable financing and development of mRNA manufacturing capabilities.

Innovative Financing Models: Adoption of innovative financing mechanisms and blended finance models is essential to support nascent industries in LMICs.

Ecosystem Development: A holistic approach encompassing R&D, manufacturing, regulatory support, and market access is necessary to build sustainable vaccine production ecosystems.

Public-Private Partnerships: Strengthening public-private partnerships can enhance investment security and support long-term development goals.

Government Role: Governments play a pivotal role in creating favorable policies and securing procurement commitments to support local manufacturers.

Conclusion

The meeting underscored the need for a concerted effort to develop innovative financing models and strengthen the ecosystem for mRNA technology in LMICs. The discussions highlighted the importance of collaboration, sustainability, and strategic partnerships in achieving equitable and resilient vaccine manufacturing capabilities globally. The event marked a significant step towards engaging MDBs and stakeholders in advancing mRNA technology to address global health challenges

Introduction

Vaccines have been crucial in saving millions of lives every year, making them a vital part of the world's public health success stories. They are cost-effective, improve life expectancy, and contribute to economic growth*[1]*. However, the progress in vaccinations varies greatly across countries, particularly in low- and middle-income countries (LMICs) where vaccination rates remain low*[2]*. Despite having very high vaccination rates for routine immunization programs, the majority of LMICs, and vaccines supplied in the region are predominantly produced in a few countries. Limited geo-diversification of vaccine production contributed to the vaccine inequity experienced during the COVID-19 pandemic, as countries where vaccines are produced decided to first fulfil their own markets over ensuring global equity. Additionally, other factors, such as research and development (R&D), production, supply, acceptance, and administration of vaccine products worldwide, also affect disparities in vaccine access*[3]*. Consequently, the new emphasis on local (and regional production) emphasizes the need for interested countries to also strengthen R&D, innovation, and capacity-building to achieve sustainable vaccine production during inter- and intra-pandemic times. Proper ecosystem development is essential, and financing plays a crucial role.

The COVID-19 pandemic highlighted the unequal landscape regarding vaccine distribution. Only a few countries were actively involved in vaccine development and manufacturing, which led to a new emphasis on local production. Interested countries need to work on technology transfer/assimilation, innovation, and capacity-building to achieve sustainable vaccine production during inter- and intra-pandemic times. Proper ecosystem development is essential, and financing plays a crucial role*[4].*

Vaccine research, development, and manufacturing require significant capital, ranging from tens to hundreds of millions of dollars. While the financial commitment is substantial, the potential returns are equally significant. Sustainable vaccine manufacturing requires continuous development, production, and supply of safe, effective, and affordable vaccines globally. To achieve this, organizations must have viable business models and incentives to manufacture vaccine products. This presents a unique opportunity for stakeholders to invest in a sector that not only promises financial gains but also contributes to global health security *[4,5]*.

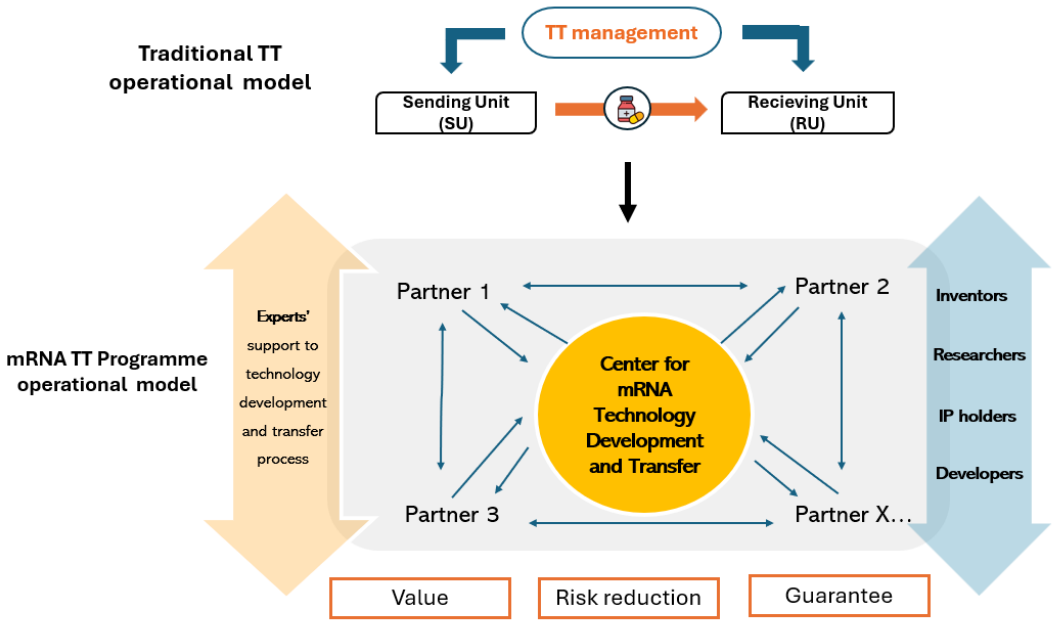
The potential of the messenger ribonucleic acid (mRNA) technology for rapid scale-up and production of safe and effective vaccines was demonstrated during the COVID-19 emergency response, making it a promising tool to ensure equitable and global access to vaccine manufacturing and pandemic response*[6].*

The mRNA Technology Transfer Programme (mRNA TT Programme) was launched in 2021 as a response to the global COVID-19 vaccine access inequity. It is a collaboration between WHO, the Medicines Patent Pool, and private and public partners from 15 LMICs in Africa, Asia, Europe, and South America. It aims to enable autonomy in the development, manufacture, and distribution of mRNA vaccines in LMICs. One of the programme's expected results is to contribute to the overall improvement of health and health security in LMICs through equitable access to mRNA-based vaccines*[6,7]*.

The mRNA TT Programme differentiates from traditional models of technology transfer (unidirectional) by operating in a global collaborative network driven by a multilateral

technology transfer approach, empowering its partners to gain know-how and absorb technology (Figure 1). The unwillingness to share the know-how of established mRNA technology required the program partners to establish mRNA technology, thus fostering a predominantly South-South mRNA R&D collaboration. The program aims to fulfil two complementary general objectives of a) establish and/or enhance sustainable mRNA vaccine manufacturing capacity; and b) develop skilled human capital in the regions where mRNA vaccine manufacturing capacity is established and/or enhanced*[7,8].*

Figure1: mRNA Technology Transfer Programme operational model. TT: technology transfer.



The mRNA technology transfer program has made substantive progress in building up a network of partners in 15 countries to acquire mRNA technology to produce vaccines. In addition, four regional R&D consortia have been established in Asia to advance research on new mRNA vaccines, for dengue, hand-foot and mouth disease (caused by enterovirus-A 71 (EV-A71), malaria (caused by plasmodium vivax) and (therapeutic human papillomavirus). Given that mRNA has extensive market potential across various disease areas, WHO is convening sessions for multilateral development banks to be introduced to the program partners and raise awareness of upcoming investment opportunities*[9].*

On April 17th, 2024, a hybrid meeting was held during the World Bank Spring Meetings by the World Health Organization (WHO), the Pan American Health Organization (PAHO), and the Medicines for Patent Pool (MPP). The meeting's purpose was to discuss the potential for multilateral development banks to invest in mRNA-based technologies in LMICs. This investment can help improve pandemic preparedness and response and address unmet public health needs.

The event brought together partners of the mRNA TT Programme and representatives from multilateral development banks to discuss the financial support required for expanding vaccine pipelines and pandemic capacity. It provided an opportunity to discuss sustainable financing for mRNA-based products across the value chain (Figure 2). The event sessions highlighted the importance of transferring platform technology, and showcased multilateral development

banks' instruments for funding research, development, and manufacturing of health products in LMICs. It also promoted the sharing of experiences related to challenges faced by biomanufacturers in LMICs and challenged the status quo to finance the expansion of biomanufacturing capacities in LMICs by discussing innovative ideas.

Figure 2: Group photo of meeting in-person participation.

Investment models of multilateral development banks for local manufacturing of health product

This meeting session was focused on the presentation of instruments to fund research, development, and manufacturing of health products in LMICs. It was a panel where representatives from multilateral development banks had the opportunity to discuss their current approach and outline the existing barriers and needs they face when considering new investments in health product development projects in LMICs (Figure 3).

Figure 3: session panel of speakers from multilateral development banks moderated by Ike James, Medicines Patent Pool.

The discussions considered the dynamics of the mRNA TT Programme as the starting point. In that case, it is important to recognize that technology transfer cannot occur in isolation but requires an ecosystem which considers elements such as R&D and manufacturing within these ecosystems. Establishing manufacturing capacity takes time, as does bringing a product to commercial launch, underscoring the urgency of initiating these processes now for future pandemic preparedness.

Moreover, there is need for inter-pandemic sustainability once these manufacturing facilities and ecosystems are operational. This requires maintaining readiness for future pandemics, which necessitates measures such as establishing product pipelines, forming R&D consortia, and the ability to license products from other sources.

Looking ahead, the discussion of this panel session aimed to explore various instruments for investing in R&D and manufacturing of health products, particularly LMICs. The focus lay not only on fostering innovation and development within the health sector but also on improving access to essential medicines and health technologies in regions where they are most needed. This holistic approach seeks to address both immediate needs and long-term sustainability in global health preparedness and accessibility.

Overall, the panel highlighted the critical importance of creating bankable projects within multilateral development banks (MDBs), not just for immediate commercial gains but for fostering sustainable capabilities that can outlast current resources. They emphasized the need to shape markets towards sustainable and commercially viable regionalized medical manufacturing ecosystems. This entails investing not only in capacities like infrastructure and equipment but also in broader capabilities such as human capital, regulatory resources, access to technology, delivery and quality control, and procurement and financing capabilities.

While MDBs have supported local manufacturers in developing countries for decades, they face challenges, especially regarding technology risks. The panelists called attention for better collaboration among MDBs to pool complementary resources and increase their risk appetites to better support the sector. Sustainability emerged as a common challenge, extending beyond financial viability to encompass the ability of initiatives to outlast current political will and resources.

Regarding financing models, the presentations advocated for time-bound market-shaping initiatives and milestone payments to incentivize eventual commercial viability. They also stressed the importance of reducing dependency on certain markets, particularly in manufacturing and technology, to achieve fully self-sustained ecosystems. This entails democratizing innovation by fostering regional incubation and developing technologies tailored to the needs of developing countries. The panelist emphasized the significance of platforms like the discussed one in achieving this goal.

The Asian Infrastructure Investment Bank (AIIB) acknowledged its newcomer status in the health sector among MDBs and its ongoing preparation of a health strategy. They recognized the increasing interest of developing countries in local pharmaceutical manufacturing, particularly post-pandemic. With diverse demands ranging from active pharmaceutical ingredients (APIs) to vaccines, AIIB noted the challenges posed by clients in weaker financial positions, especially in Africa and frontier line countries.

Acknowledging the conservative nature of MDBs in supporting well-established companies, AIIB emphasized the need for a higher risk appetite to finance dynamic and innovative players in the health sector, particularly in developing countries. They highlighted the necessity of blended finance to support such ventures. Moreover, AIIB discussed the potential of South-South cooperation to promote connectivity and technology transfer among member countries. They shared their involvement in Central Asia to develop local manufacturing capacity, noting challenges such as small national markets and regulatory harmonization issues inhibiting regional market development. They emphasized the importance of regional markets for health products to address challenges faced by small markets.

Innovative financing mechanisms, such as the front-loading facility for GAVI and sovereign bond swap discussions under the G20, were highlighted as means to support emerging and weak manufacturing sectors or procure vaccines using public funds. The existing limitations of sovereign operations in enabling market conditions for local manufacturing were pointed out as the need for leveraging private sector operations.

The Inter-American Development Bank (IDB) emphasized collaboration aimed at creating impactful value, in line with their model of "improving lives." With vaccines, the implicit goal is preserving lives, especially in the most affected regions. The IDB expressed a willingness to take on slightly higher risks but expects repayment, insisting that their financing terms remain commercial yet flexible to ensure project viability.

They outlined four key aspects crucial for analyzing projects: the experience and credibility of sponsors, the mitigation and analysis of market risk, construction risk, and sustainability. Sponsors must be prepared to handle unforeseen challenges and have the necessary resources to support projects. Market risk, akin to financing a power plant for future needs, requires robust models and alignment with Good Manufacturing Practices (GMPs).

Construction risk factors in the experience and technology of builders and aligning with the project's developmental stage. The IDB is open to funding early-stage R&D with grants or later-stage clinical developments with equity, but clear exit strategies are essential. Flexibility in partnerships and long-term horizons are vital due to the nature of infrastructure projects, often requiring extended construction periods and grace periods.

Capacity building is crucial, focusing on the right scale and ensuring sustainability remains central to all endeavors. Acknowledging the diverse perspectives on sustainability, the IDB stressed the importance of collaboration to approach sustainability from various angles, leveraging technical expertise from partners like PAHO.

Finally, the International Finance Corporation (IFC) pointed out that since the pandemic, they expanded their scope to include partnerships with different stakeholders. This broadening of focus was enabled by their upstream capabilities and the evolving business environment catalyzed by Covid-19.

Ensuring inclusivity of all partners, not just established players, requires a shift in approach from transactional to strategic. This involves developing strategies and partnerships and expanding the toolkit beyond financing to include support in various forms, such as technical expertise and supply chain sustainability.

The IFC discussed the importance of derisking models, both financial and non-financial, to strengthen proposals that may not meet all criteria. Programs offering technical capabilities and market access signal strong support and provide comfort to financiers.

Blended finance models, combining different financing mechanisms, are crucial for catalyzing more financing, particularly in Africa. The IFC proposed using grant funding for guarantees instead of direct financing, allowing companies to share risks and potentially access commercial or public financing.

Innovative financing models, such as using public financing for vaccine manufacturing with repayment upon success, are explored to enable companies, beyond the usual suspects, to access capabilities. This diversification and democratization of capabilities aim to ensure broader participation in the Life Sciences sector across regions.

After the MDBs initial exposure, the panel discussion revolved around financing expectations, risk management, and collaboration mechanisms among MDBs, private financiers, and public sector funders. The MDBs panelists highlighted their ability to provide patient capital with longer tenors and grace periods, aligning return expectations with the risk undertaken. Flexibility in financing structures, including blended finance, aims to reduce costs and risks for companies and financiers, ensuring commercial viability while considering development impact.

Collaborative efforts between MDBs, private financiers, and public sector funders are crucial to support upstream and downstream activities in pharmaceutical manufacturing. Coordination forums have been established to map out capabilities, align interests, and leverage diverse funding sources. Early engagement between stakeholders, including MDBs, private financiers, and public sector funders, facilitates education, risk mitigation, and strategic alignment, enhancing project viability and sustainability.

The public sector, through MDBs' public sector arms, plays a pivotal role in supporting health ministries, regulatory agencies, and scientific research institutions. Collaborative efforts between MDBs and the public sector aim to fill gaps in early-stage research funding, strengthen regulatory frameworks, and coordinate vaccine distribution and market access. This integrated approach ensures comprehensive support across the pharmaceutical manufacturing value chain, fostering sustainable health ecosystems in developing countries.

Reflections on capital expenditure and operating expenditure (CAPEX-OPEX) models and estimated capacity to contribute to a pandemic response within the context of the mRNA Technology Transfer Programme

This session was an online presentation to outline the results of capital expenditure (CapEx) and capital expenditure and operating expenditure (OpEx) analysis conducted to assess the costs of establishing and maintaining mRNA production capability*[10]*, followed by recent work examining the program's potential contribution to mRNA vaccine availability in pandemic scenarios.

The CapEx and OpEx analysis evaluated the investment requirements associated with setting up and operating small-scale GMP grade mRNA vaccine facilities, considering technical requirements and production capacities along with sustainability and long-term capacity retention. The presentation emphasized that decision-making regarding facility design and specifications lies with the program partners, with the analysis providing essential information to facilitate these decisions.

The analysis focused on balancing costs and capabilities, considering a small footprint

facility focusing on the key steps in mRNA vaccine production, including transcription of mRNA itself and encapsulation to create the bulk mRNA vaccine drug substance. Other steps such as DNA template generation and fill and finish capability are excluded as they can potentially be outsourced to third parties.

Three scenarios were modeled: a standalone mRNA facility, an mRNA facility integrated into an existing vaccine manufacturer, and a flexible facility incorporating biologics manufacturing. The costs ranged from $15 to $20 million for standalone facilities, $5 to $10 million for integrated facilities, and $80to $112 million for flexible facilities. Operational expenses varied across the scenarios, with annual mRNA production of 200,000 doses for each, with a maximum capacity of 15,000,000 doses on a single shift basis which is scalable of the number of shifts in a facility can be increased.

The subsequent part of the presentation discussed the mRNA technology transfer program's potential contribution to mRNA vaccine availability during a pandemic situation and considered a future pandemic declaration at three time points: 3, 5, and 10 years from now.

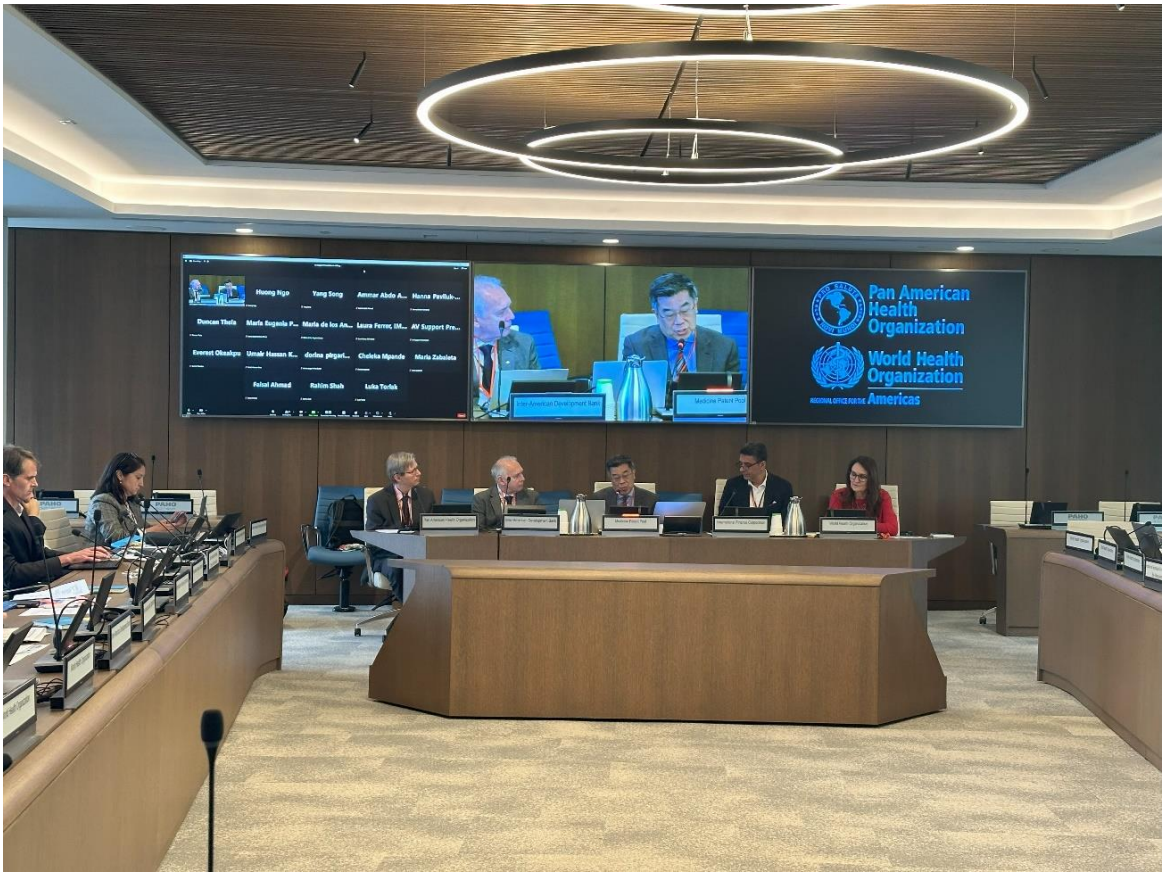
The analysis projected cumulative mRNA vaccine production from the program partners as a whole and assessed potential capacity across three basic scenarios: low, mid and high output cases. The model indicated that the cumulative, collective output from programme partners ranged from 350 million to 1.2 billion doses over an 18-month period post-pandemic declaration, and depends on various factors such as partner capabilities, production systems and underlying growth in mRNA vaccine requirements and usage. Upside factors such as an increase in the number of program partners and second-generation automated manufacturing technologies could enhance production capacity above the predicted range.

The conclusion highlighted the importance of establishing small footprint facilities to balance investment costs with production capacity, maintaining production capability across partners, exploring additional revenue streams to support the ongoing costs of retaining capacity, fostering R&D collaborations to drive development of mRNA products for inter-pandemic use, and recognizing the program's potential to generate significant vaccine production during pandemics. Pandemic modelling projections for the high output scenario indicated the potential for the programme as a whole to deliver 600 million to 1.2 billion doses within a 10-year timeframe.

Building the ecosystem for the development of new mRNA-based products in LMIC

This panel focused on addressing issues related to the research and development of new mRNA products and how MDB and partners can contribute to creating a sustainable investment. It highlights the discussion on building an ecosystem for the development of new mRNA-based products in LMICs, acknowledging the privilege of having a diverse panel comprising manufacturers and financial institutions (Figure 4).

Figure 4: session panel of speakers moderated by Professor Anthony So, Johns Hopkins Bloomberg School of Public Health.



The focus of the session was to discuss ways to address barriers and opportunities in the R&D of mRNA products, particularly vaccine technology, which holds significant promise for public health due to its versatility in targeting various diseases. The importance of sustainable investment in both pandemic and endemic disease targets is emphasized, as the need to widen the window of risk for financial investments to accommodate nascent manufacturing capacities.

The representative from Afrigen was asked to comment about "what are the challenges that you encountered and what has been helpful to overcome them and how did they secure investments for the growth of Afrigen to be able to expand into mRNA technology". She begins by highlighting the significance of derisking mRNA capabilities in LMICs, particularly in Africa, due to the support of the Programme. She then delves into the challenges faced during the development of mRNA technology, emphasizing the time constraints and the need for rapid skills development, equipment access, and facility

establishment. Despite these challenges, they view the process as an opportunity for progress and growth.

Budget constraints emerge as another major challenge. The panelist underscores the importance of meeting diverse expectations for the program while navigating various stakeholder interests. They emphasize the necessity of collective effort and collaboration among partners to ensure the sustainability of mRNA technology for public health purposes.

Furthermore, the panelist discusses Afrigen's unique position as a biotechnology start-up company, emphasizing its mission to localize vaccine manufacturing for the African continent. They outline the role of development finance institutions in supporting Afrigen's growth, with a focus on long-term vision and strategic equity partnerships to secure funding. Despite being pre-revenue earnings, Afrigen aims for sustainable growth through a combination of shareholder investment and non-dilutive funding.

In terms of securing investments, Afrigen relies on strategic shareholders with a strong understanding of the company's mission and its potential to contribute to economic development in South Africa and beyond. The panelist stresses the inherent value of mRNA technology in both public health and commercial sustainability, underscoring the importance of strategic partnerships and long-term vision in securing funding for Afrigen's growth and expansion into mRNA technology.

Institute Pasteur Tunis (IPT) was invited to comment on the difficulties in convincing domestic and international funders to provide capital and running costs for research into new products and what other sources of revenue the institution was considering. They discuss the establishment of a mRNA tech transfer initiative within their institute in 2021, with a focus on capacity building, research, and development of mRNA vaccines and therapeutics for prevalent diseases in LMICs. They cite collaborations with organizations like Moderna and the Bill & Melinda Gates Foundation to develop mRNA vaccines against diseases like leishmaniasis and rabies. Moreover, they highlight their participation in initiatives aimed at improving health security in LMICs and establishing sustainable regional production of mRNA vaccines, particularly in response to the COVID-19 pandemic.

Furthermore, the representative mentions a project funded by the European Commission focused on training the workforce in mRNA technology. This project covers the entire process from research and innovation to market access, reflecting their institute's commitment to advancing mRNA technology and ensuring its widespread adoption in LMICs. Through these initiatives and collaborations, IPT seeks to secure funding for research into new products and explore alternative revenue sources to support their efforts in advancing mRNA technology for public health.

The debate continued with the perspective of the Islamic Development Bank (IsDB) on how MDBs banks ensure coherence between the private sector and public sector lending, i.e., the public sector is a potential buyer of locally produced products, the public sector can also play a pivotal role in increasing skills needed for R&D and manufacturing. They emphasize the complexity of mRNA technology transfer, noting that each country must

undergo its vaccine development process, which typically takes between 5 and 7 years. Financing such long-term projects presents a significant challenge due to capacity constraints and uncertain future demand.

The IsDB representative shares their experience in supporting vaccine development and diagnostics during the COVID-19 pandemic, acknowledging the need for comprehensive financing packages involving governments, philanthropists, the private sector, and other international organizations. They stress the importance of regional vaccine supply and the introduction of new vaccines, underscoring the need for coordinated planning and support.

Moreover, they discuss the potential recipients of IsDB support, highlighting existing vaccine suppliers in member countries such as Indonesia, Tunisia, and Bangladesh, while also identifying greenfield opportunities for vaccine production. They emphasize the importance of supporting national regulatory agencies to ensure the quality and sustainability of local pharmaceutical industries.

The representative outlines a business model for vaccine development and procurement, emphasizing the need for collaboration with organizations like the WHO and regional bodies such as the African Union. They propose a multifaceted approach involving support for research and development, technology transfer, procurement, and vaccine delivery.

In conclusion, the IsDB representative underscores the importance of strong partnerships and collaboration between development banks, governments, and other stakeholders to address the challenges and opportunities in vaccine development and production. They highlight ongoing initiatives with partners like the African Development Bank and the European Investment Bank, demonstrating their commitment to advancing health-impact investment in their member countries.

Bio-Manguinhos followed the discussion to provide the perspective of a public manufacturer. They were asked to comment on the role of public-private partnerships to encourage the development of new products. They stressed that as a governmental company operating within the public sector, it faces restrictions on funding, only being eligible for non-refundable funds. To overcome this limitation, they explore various alternative funding sources available in Brazil. These include internal innovation programs, funds from the Ministry of Health, programs from the Brazilian Development Bank, and financing from agencies like Finap. Additionally, they mention receiving funds from private companies and non-profit organizations, such as donations from Germany.

Regarding partnerships, Bio-Manguinhos emphasizes its long tradition of collaborating with both big pharmaceutical companies and smaller firms. They highlight the importance of partnerships in accelerating the development process by pooling knowledge and resources. Brazil has specific programs designed to foster public-private partnerships, and Bio-Manguinhos has benefited from these initiatives in developing new products, such as the back Emir vaccine.

Despite advancements in their vaccine program, they acknowledge the challenges

associated with technology transfer, emphasizing the need for a conducive ecosystem involving expertise in manufacturing, quality control, and regulatory affairs. Bio-Manguinhos expresses its commitment to sharing its expertise with partners and discusses the potential for technology transfer partnerships once its vaccine development project reaches success. Their role within pandemic preparedness for Brazil involves active participation in initiatives like the mRNA program, with a strong commitment to ensuring its success.

Finally, closing this panel the International Finance Corporation provided input regarding how the institution supports investments related to R&D by clients or encourages collaboration with public research centers. While not focusing on financial instruments, the speaker addressed key elements in the paradigm shift brought about by platforms like mRNA technology. They emphasized the importance of R&D and research in this new paradigm, highlighting the need for models to support R&D, particularly in developing regions like Africa. The speaker underscores the diversity of models and the necessity to tailor approaches to individual circumstances, noting that there is no one-size-fits-all solution, especially regionally.

The absence of certain stakeholders, notably governments and venture capital development equity funds, is highlighted as a limitation in the current landscape. The speaker stresses the critical role of governments in setting priorities and allocating funding for R&D, citing examples like Brazil and Korea, which invest significantly in research. They advocate for increased government investment in R&D, even if it means redirecting funds from other projects, as it can yield substantial long-term benefits. Additionally, the importance of venture capital and private equity funds with a focus on development investment is emphasized for fostering innovation and sustainability.

The speaker acknowledges the complexity of R&D funding and the need for a comprehensive business plan that considers the entire development pathway. They emphasize the importance of understanding the investment required at each stage of development and identifying potential beneficiaries to attract funding. The role of development finance institutions (DFIs) is discussed, highlighting their approach of investing in funds with multiple opportunities for returns to mitigate risks. Finally, the speaker emphasizes the need for collaboration among various stakeholders, including government agencies, private companies, and research institutions, to leverage resources and expertise effectively in advancing R&D initiatives.

Addressing the needs of a nascent mRNA industry in LMIC

The 15 program partners have varied experiences in vaccine (and other health products) manufacturing, resulting in both shared and unique challenges and expectations for support. In this session, panelists reflected on policy enablers for establishing a new vaccine manufacturing industry and provided lessons learnt based on ongoing partnerships with their government and within the region (Figure 5). The role of governments emerged as a common enabler for supporting the establishment of a new ecosystem.

Figure 5: session panel of speakers moderated by Ariane Abreu, World Health Organization.

Biovax, based in Kenya, shared their experiences securing the capital required to establish a new (mRNA) vaccine manufacturing facility. As a new entity, they emphasized the importance of governments and funding institutes to recognize and understand the unique challenges new biomanufacturers encounter. Specifically, the need for major financial investment before any products are available on the market may not align and

reconcile with the immediate needs of the government and poses a challenge with securing governmental funding. Biovax also emphasized that financing and investment mechanisms should consider an ecosystem approach that includes biomanufacturing workforce recruitment and capacity development, defining regulatory processes, and strengthening the regulatory system, especially in establishing a nascent industry.

Sinergium, based in Argentina, highlighted that enabling policies and private-public partnerships can provide the necessary security to secure non-governmental investments. They discussed how successfully securing long-term (10-year) procurement commitments from the Argentinian government played a crucial role in shaping demand and ensuring local manufacturing efforts strategically aligned with national and regional strategies. These commitments supported risk mitigation and provided the assurance for financing infrastructure development Singergium needed to establish new vaccine manufacturing facilities. Further, guaranteeing a secure and stable market enabled them to reduce the cost of goods through facilitating economies of scale.

Biovac (based in South Africa) also reflected on their experience, highlighting that "...manufacturing exists in an ecosystem, we can focus on the cost of goods, having the raw material (e.g. LNP). However, if the market is not receptive and ready to buy the products, these efforts will be in vain". They emphasized that though procurement commitments by governments can support the manufacturer's growth, negotiating longer-term commitments that can support long-term financing is crucial. - "manufacturers have more financial bargaining leverage with a 10-year vs 2-year procurement commitment".

Additionally, procurement commitments and future procurement arrangements should consider a whole-of-government approach that accounts for policy changes. The ministerial entities that support industry growth are not the same as those that define health policies. It is important to ensure that all arms of government are informed of potential policy changes to ensure local manufacturers can revise strategies to compete for tenders that ensure the health systems are supplied with the health products they need.

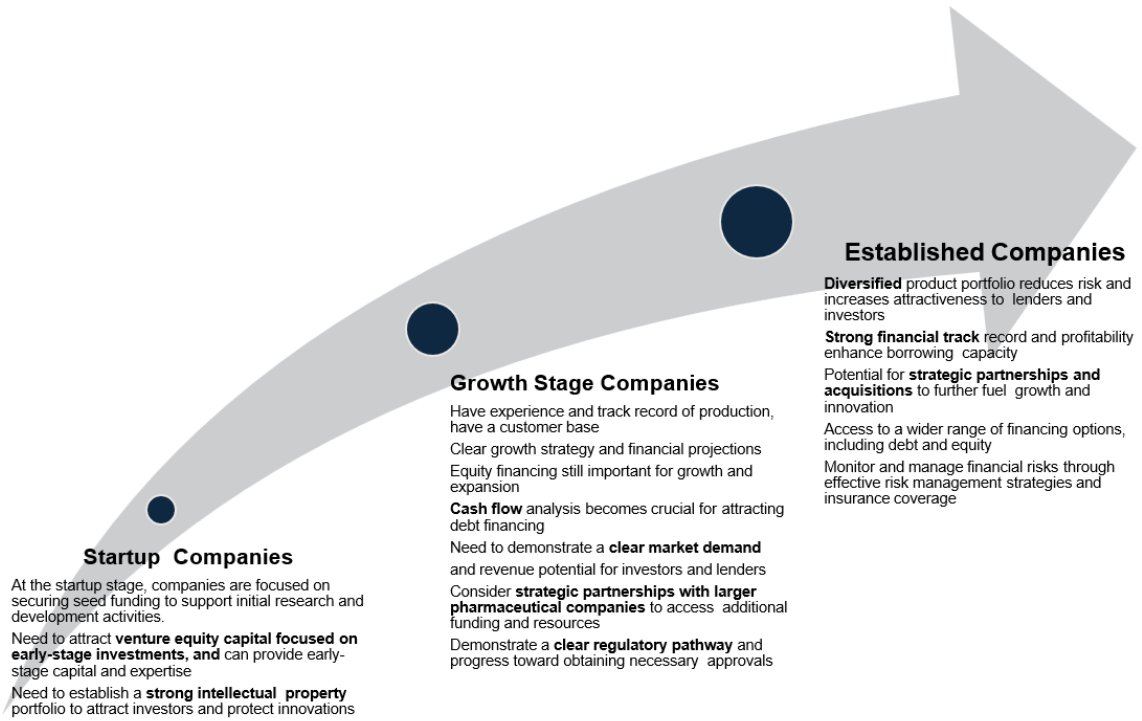
Even with government support, local demand may not be sufficient for some manufacturers to maintain sustainability, particularly for manufacturers based in small countries. Consequently, new manufacturers must ensure they can secure local and regional market demand. Torlak remarked that even securing regional demand can be challenging for manufacturers entering the market. He emphasized the need for favourable policies such as trade agreements to support regional procurement, particularly when there is an increase in demand—more doses enable reduced fixed costs.

A major lesson learnt during the COVID-19 pandemic is the importance of health security. Even though technology transfer (TT) initiatives do positively contribute to the manufacturing ecosystem, these initiatives primarily focus on supplying the local markets as there are typically no incentives for the owners of the IP and know-how to leverage this partnership to supply the region, as "they" the owners can directly negotiate with regional procurers such as GAVI. Further, TT partnerships could be limiting as they may not necessarily foster the R&D needed to develop your own products eventually. The hope is that with new initiatives such as the African Vaccine Manufacturing Accelerator (AVMA),

there will be more incentives for partnerships with local manufacturers to supply the region – with a specific emphasis on procuring locally/regionally produced products to supply the regional and global markets.

The last panellist in this session, IFC, discussed financing instruments that could support the nascent industry, highlighting that approaches to financing local manufacturers should be multifaceted and consider the manufacturer's maturity level. Parameters for consideration include the product's scalability, access to markets, and the type of funding needed (angel [grant] funding v. equity investment), and strategic partnerships to facilitate manufacturing capabilities need to be considered, among others. The ability to attract investors and the type of investment likely to support manufacturers' growth and loan repayment capacity varies depending on the maturity of the manufacturer (as illustrated in Figure 6)

Figure 6: Considerations of biomanufacturers' maturity, financing mechanisms, and opportunities to support financing manufacturers.



It's a common narrative that manufacturers primarily consider banks for financing the nascent industry. However, this perspective must evolve to encompass the broader

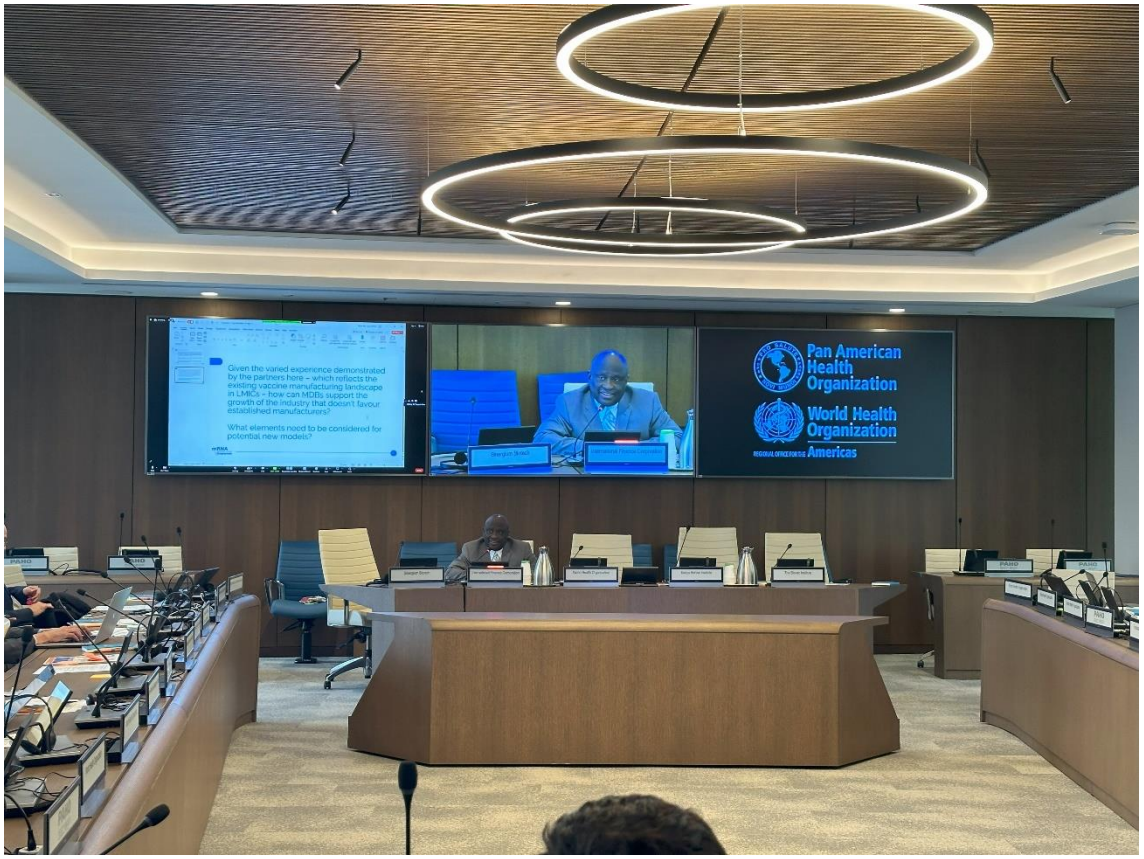
funding landscape, including non-MDB or commercial banks, to ensure a diverse and robust financial strategy. For new manufacturers (start-ups), angel investors who are not expecting a product or commercial return, i.e. financially backing your idea and principle—similar to investing in R&D—would be the ideal target for funding. IFC emphasized that these types of investors are funding your potential for R&D to generate IP and know-how that can eventually lead to a valuable, commercially viable product. Often, MDBs are not the ideal target for supplying this type of capital. However, MDBs and multilateral institutions can support crowd-funding initiatives to have a general pool of funding that can be leveraged- and enable the growth of new manufacturers without needing to pay back loans.

As manufacturers grow and gain capabilities to produce commercially viable, quality-assured products, they may become more eligible for MDB and DFI financing. A key enabler is the need for strategic partnerships to support product manufacturing and regulatory pathways to ensure quality assurance of products. Moreover, the scalability and market access of manufactured products are critical considerations. IFC emphasized that aggregation of markets emerges as a key strategy for mitigating financial risks and enhancing returns on investment – this underscores the need for strategies to support regionalized manufacturing capacity to supply regional markets.

Envisaging new financing models for LMIC-based manufacturers

IFC started the session by requesting manufacturers to reflect on what can be done differently to reduce the impediments and barriers new manufacturers face in securing funding (Figure 7). The previous sessions highlighted an ecosystem approach and the importance of consortia and collaborations.

Figure 7: discussion session lead by Ken Osei, International Finance Corporation



There is an art to raising funding, and biomanufacturers also need to reflect on how to raise funding, develop strategies for commercializing products, and build partnerships for R&D and manufacturing. A reflection by Biovac highlighted the need to know who to target and what language to use. A blended approach to securing financing, for example, a combination of grant funding and MDB/DFI financing to enable R&D and biomanufacturing development and the commercialization of products, could facilitate end-to-end funding.

During the COVID-19 pandemic, philanthropic funding was leveraged to support R&D and manufacturing. A mechanism similar to the pandemic fund which aims to finance LMICs and regions to strengthen their capacity for pandemic prevention, preparedness, and response (link), could be developed. "Fragmentation creates opportunities for funders to have more supplier power"— a neutral global agency can strengthen biomanufacturers' procurement power for capital investment by aggregating and coordinating initiatives/consortia, which, in the process, creates greater credibility and leverage that attract funding. A specific role of MDBs in this initiative would be to develop mechanisms and partnerships that attract a pool of funds that biomanufacturers can leverage to support financing. Furthermore, aggregation should also consider the support funders (MDBs/ DFI and governmental institutions) who need to coordinate various pools of capital. It should also be considered that there might be exclusion lists for funders that may impede progress. This further emphasizes the need for neutral partners to ensure organization and enable support for all.

Closing remarks

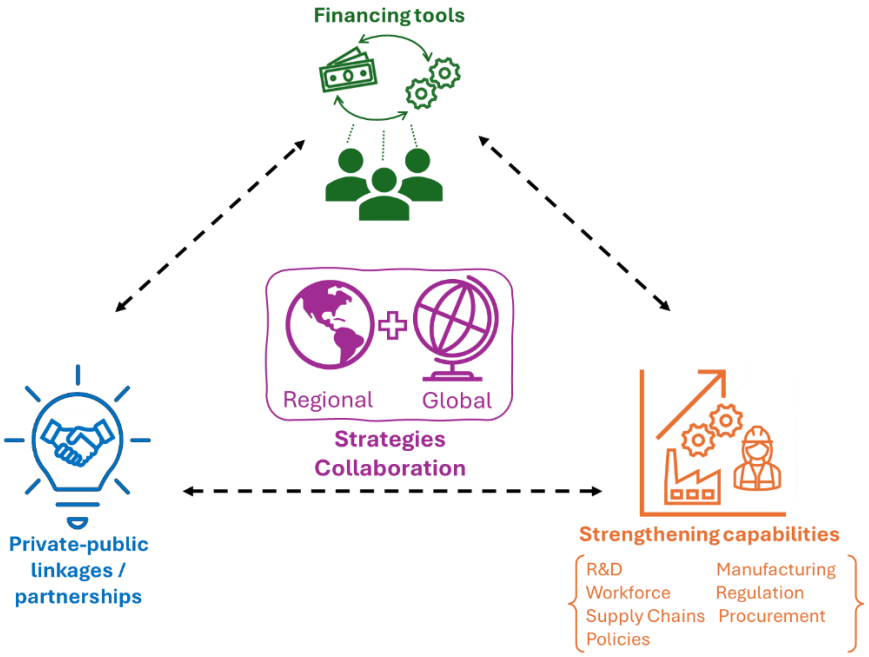
The convening of this meeting marked an inaugural opportunity to engage in discussions regarding sustainable end-to-end financing along the value chain of mRNA-based products. Rather than focusing solely on product transfer, the emphasis lies on platform technology transfer, heralding a new model for advancing mRNA technology. The early stages of mRNA technology were underscored by the groundbreaking potential demonstrated by the COVID-19 mRNA vaccine, igniting efforts to democratize access to mRNA technology through collaboration and network building. Despite the challenges, manufacturing panelists expressed optimism. They emphasized the major benefits of being part of a multilateral TT program: collaboration, coordination, and the consortium approach applied to the mRNA program, which supports the sharing of ideas and knowledge that contributes to increased yield and

lowered production costs. Any breakthrough and improvements by one manufacturer can benefit all and lower production costs. Lastly, 15 partners being in strategic regional entities further reduces competition and also allows for regional supplies of products when they become available.

Amidst technological advancements, there is a pressing need to develop innovative financing models to support these endeavors. Notably, this meeting represents the first gathering of all multilateral development banks to deliberate on bolstering mRNA production capacity, setting the stage for an essential dialogue among a diverse array of partners. As the technological landscape evolves, it becomes evident that our thinking must adapt accordingly.

Key themes emerging from this dialogue include the imperative to rethink financing tools, with multilateral development banks prepared to adjust their strategies to accommodate the public good component inherent in mRNA production. Moreover, there is a recognition of the pivotal role of the public sector in facilitating the flourishing of mRNA technology, necessitating a better understanding of public-private linkages. Furthermore, the value of local manufacturing must be factored into funding evaluations, considering its dual role in addressing local health needs and responding to pandemics, and support should encompass a whole of government approach, including industry, infrastructure, regulations and health policies.

Figure 8: Key themes highlighted as enablers for sustainable end-to-end biomanufacturing


Financing tools
Regional
Global
Strategies
Collaboration
Private-public
linkages /
partnerships
Strengthening capabilities
R&D
Workforce
Supply Chains
Policies
Manufacturing
Regulation
Procurement

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